Access DB#	

SEARCH REQUEST FORM (STIC)

Art Unit: 1653 Phone number: 571-272-0952 Scrial Number: 09-581397 Mail Box: 3-C-70 Examiner Rm: 3-B-75 Results format: paper *********** Title: Neuroprotective Agents Applicants: SUNDSTROM, LARS ERIC; IANNOTTI, FAUSTO; BRADLEY, MARK; PRINGLE, ASHLEY KER Earliest Priority Date: 12/16/97 ********** Applicants are claiming the compounds on the attached sheet. R² = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); R³ = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); p = an integer of 3 or 4; q = an integer of 3 or 4 Starcher Phone R	Requestor's N	ame: David Lukton	Examiner number	er: 71263 <u>Dat</u> 5 - 11 -	_
Title: Neuroprotective Agents Applicants: SUNDSTROM, LARS ERIC; TANNOTTI, FAUSTO; BRADLEY, MARK; PRINGLE, ASHLEY KER Earliest Priority Date: 12/16/97 ********** Applicants are claiming the compounds on the attached sheet. R² = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); R³ = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); p = an integer of 3 or 4; q = an integer of 3 or 4 STAFF USE ONLY Type of Search Vendors and cost where applicable and integer of the searcher Proce * As Sequence (#) Dialog Searcher Proce * As Sequence (#) Queste/Orboi Dute Searcher Decked Up Biologists Searcher Proce & Surveiure (#) Queste/Orboi Dute Searcher Decked Up Biologists Searcher Proce & Biologists Lingston Levisoness Searcher Proce & Review Time Fullicat Sequence Systems Searcher Proce & Review Time Pagent Family WWW/mement	Art Unit: 165	Phone number:			
Applicants: SUNDSTROM, LARS ERIC; TANNOTTI, FAUSTO; BRADLEY, MARK; PRINGLE, ASHLEY KER Earliest Priority Date: 12/16/97 ********** Applicants are claiming the compounds on the attached sheet. R² = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); R³ = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); p = an integer of 3 or 4; q = an integer of 3 or 4 STAFF USE ONLY Type of Search NA Sequence (#) Starcher NA Sequence (#) Starcher Profe # AA Sequence (#) Date Searcher Picked Up Date Sea	Mail Box: 3-C	2-70 <u>Examiner Rm</u> :	3-B-75 <u>Res</u>	sults format: paper	r
Applicants: SUNDSTROM, LARS ERIC; TANNOTTI, FAUSTO; BRADLEY, MARK; PRINGLE, ASHLEY KER Earliest Priority Date: 12/16/97 ********** Applicants are claiming the compounds on the attached sheet. R² = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); R³ = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); p = an integer of 3 or 4; q = an integer of 3 or 4 STAFF USE ONLY Type of Search NA Sequence (#) Starcher NA Sequence (#) Starcher Profe # AA Sequence (#) Date Searcher Picked Up Date Sea		***	*****		
Earliest Priority Date: 12/16/97 ********* Applicants are claiming the compounds on the attached sheet. R ² = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); R ³ = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); p = an integer of 3 or 4; q = an integer of 3 or 4 Starcher NA Sequence (#) STN Searcher NA Sequence (#) Dialog Scarcher Phone # A Sequence (#) Questel/Orbin Dute Searcher Phote d Up Bibliographic Dr. Link	<u>Title</u> : 1	Neuroprotective .	Agents		
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Applicants are claiming the compounds on the attached sheet. R ² = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); R ³ = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); p = an integer of 3 or 4; q = an integer of 3 or 4 STAFF USE ONLY Type of Search Vendors and cost where applicable searcher NA Sequence (#) STN Searcher Phone # AA Sequence (#) Dialog Searcher Location: Surueture (#) Questel/Orbit Date Searcher Picked Up Bibliographic Dr.Link and Completed: Latigation Lexis/Nexis Searcher Prop & Review Time Fulliext Sequence Systems Clerical Prop Time New Patent Family WWW/Internet Clerical Prop Time New Patent Family WWW/Internet WWW/Internet WWW/Internet	Earliest Priori	ty Date: 12/16/97			
Applicants are claiming the compounds on the attached sheet. R ² = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); R ³ = hydrogen or alkyl or acyl or R-NHCO- (R = alkyl or aryl); p = an integer of 3 or 4; q = an integer of 3 or 4 STAFF USE ONLY Type of Search Vendors and cost where applicable searcher NA Sequence (#) STN Searcher Phone # AA Sequence (#) Dialog Searcher Location: Surueture (#) Questel/Orbit Date Searcher Picked Up Bibliographic Dr.Link and Completed: Latigation Lexis/Nexis Searcher Prop & Review Time Fulliext Sequence Systems Clerical Prop Time New Patent Family WWW/Internet Clerical Prop Time New Patent Family WWW/Internet WWW/Internet WWW/Internet		* * *	*****	STIC	
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Inventor Search

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11/05/2004

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L42 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:753643 HCAPLUS

DOCUMENT NUMBER: 140:280736

TITLE: Characterisation of a novel class of polyamine-based

neuroprotective compounds

AUTHOR(S): Pringle, Ashley K.; Morrison, Barclay;

Bradley, Mark; Iannotti, Fausto;

Sundstrom, Lars E.

CORPORATE SOURCE: Clinical Neurosciences, University of Southampton,

Southampton, SO16 7PX, UK

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2003),

368(3), 216-224

CODEN: NSAPCC; ISSN: 0028-1298

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal LANGUAGE: English

Prolonged cerebral ischemia initiates complex intra- and inter-cellular signalling cascades ultimately resulting in neuronal death. Well-characterised mediators of ischemic cell death are glutamate, free radicals and nitric oxide. Many drugs that block these mechanisms are neuroprotective in vitro, but have unfavorable side-effect profiles in man. We have recently demonstrated that the compound L-arginyl-3,4spermidine (L-Arg3,4) is neuroprotective in vitro through an interaction with several of these mechanisms, and prevents ischemic neurodegeneration in vivo with no gross side effects. In this study, we have used solid-phase combinatorial chemical, to synthesize a number of analogs of L-Arg3,4, and investigate the structure-activity relationship using an in vitro, organotypic hippocampal slice culture model of cerebral ischemia. A number of mol. features were identified which were essential for the neuroprotective activity including the requirement for a pos. charge and an amino acid in the L-configuration. Relatively minor alterations to both the terminal arginine and polyamine moieties significantly attenuated neuroprotective efficacy. Our data implies that these compds. are neuroprotective through a currently undefined mechanism rather than non-specific ionic interactions described previously for other

CC 1-3 (Pharmacology)

ST structure activity neuroprotectant polyamine ischemia brain hippocampus IT Brain

(hippocampus; structure and neuroprotective activity of polyamine-based L-arginyl-3,4-spermidine analogs)

IT Brain, disease

(ischemia; structure and neuroprotective activity of polyamine-based L-arginyl-3,4-spermidine analogs)

IT Cytoprotective agents

(neuroprotective; structure and neuroprotective activity of polyamine-based L-arginyl-3,4-spermidine analogs)

IT Structure-activity relationship

polyamine-containing compds.

(structure and neuroprotective activity of polyamine-based L-arginyl-3,4-spermidine analogs)

IT 134950-93-9 134951-15-8 141997-14-0

191277-14-2 227758-27-2 227758-28-3

227758-29-4 227758-36-3 227758-40-9

227758-41-0 675606-34-5 675606-35-6

675606-36-7 675606-37-8 675606-38-9

675606-39-0 675606-40-3

RL: PAC (Pharmacological activity); BIOL (Biological study) (structure and neuroprotective activity of polyamine-based

L-arginyl-3, 4-spermidine analogs) 134950-93-9 134951-15-8 141997-14-0 ΙT 191277-14-2 227758-27-2 227758-28-3 227758-29-4 227758-36-3 227758-40-9 227758-41-0 675606-34-5 675606-35-6 675606-36-7 675606-37-8 675606-38-9 675606-39-0 675606-40-3 RL: PAC (Pharmacological activity); BIOL (Biological study) (structure and neuroprotective activity of polyamine-based L-arginyl-3,4-spermidine analogs) 134950-93-9 HCAPLUS RN Pentanamide, 2-amino-5-[(aminoiminomethyl)amino]-N-[4-[(3-CN aminopropyl)amino]butyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_3$
 N
 H
 $(CH_2)_4$
 N
 H
 $(CH_2)_3$
 N
 H
 NH_2

RN 134951-15-8 HCAPLUS
CN Hexanamide, 2,6-diamino-N-[3-[(4-aminobutyl)amino]propyl]-, (2S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_4$
 N
 H
 $(CH_2)_3$
 N
 H
 $(CH_2)_4$
 NH_2

RN 141997-14-0 HCAPLUS

CN Pentanamide, 2-amino-5-[(aminoiminomethyl)amino]-N-[3-[(3-aminopropyl)amino]propyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 N_H
 $(CH_2)_3$
 N_H
 $(CH_2)_3$
 N_H
 $(CH_2)_3$
 N_H
 $(CH_2)_3$
 N_H

RN 191277-14-2 HCAPLUS

CN Pentanamide, 2-amino-N-[3-[(4-aminobutyl)amino]propyl]-5-[(aminoiminomethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

$$(CH_2)$$
 4 (CH_2) 3 (CH_2) 1 (CH_2) 1

RN 227758-27-2 HCAPLUS CN Hexanamide, 2,6-diamino-N-[3-[(4-aminobutyl)amino]propyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)_4$$
 $(CH_2)_3$ $(CH_2)_4$ $(CH_2)_4$

RN 227758-28-3 HCAPLUS
CN Pentanamide, 2,5-diamino-N-[3-[(4-aminobutyl)amino]propyl]-, (2S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_3$
 N
 H
 $(CH_2)_4$
 NH_2

RN 227758-29-4 HCAPLUS
CN Pentanamide, 2,5-diamino-N-[3-[(4-aminobutyl)amino]propyl]-, (2R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)_3$$
 $(CH_2)_3$ $(CH_2)_4$ $(CH_2)_4$

RN 227758-36-3 HCAPLUS
CN Pentanamide, 2-amino-N-[3-[(4-aminobutyl)amino]propyl]-5[(aminocarbonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

$$H_2N$$
 (CH₂) 4 (CH₂) 3 N S (CH₂) 3 N NH₂

RN 227758-40-9 HCAPLUS

CN Pentanediamide, 2-amino-N1-[3-[(4-aminobutyl)amino]propyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 227758-41-0 HCAPLUS

CN Pentanamide, 2-amino-N-[4-[(4-aminobutyl)amino]butyl]-5-[(aminoiminomethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_4$
 $(CH_2)_4$
 N
 H
 $(CH_2)_4$
 N
 H
 NH_2
 NH_2

RN 675606-34-5 HCAPLUS

CN 1H-Imidazole-4-propanamide, α -amino-N-[3-[(4-aminobutyl)amino]propyl]-, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 675606-35-6 HCAPLUS

CN Hexanamide, 2,6-diamino-N-[4-[(4-aminobutyl)amino]butyl]-, (2S)- (9CI) (CA INDEX NAME)

RN 675606-36-7 HCAPLUS

CN Pentanamide, 2-amino-5-[(aminoiminomethyl)amino]-N-(8-aminooctyl)-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_8$
 N
 H
 NH_2
 NH_2

RN 675606-37-8 HCAPLUS

CN Pentanamide, N-[3-[(4-aminobutyl)amino]propyl]-5-[(aminoiminomethyl)amino]-2-[(phenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 675606-38-9 HCAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[(4-aminobutyl)amino]propyl]amino]carbonyl]-4[(aminoiminomethyl)amino]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 N_H
 $(CH_2)_3$
 N_H
 $(CH_2)_4$
 N_H
 N_H

RN 675606-39-0 HCAPLUS

CN Pentanamide, N-[3-[(4-aminobutyl)amino]propyl]-5-[(aminoiminomethyl)amino]-2-[(phenylsulfonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 N_H
 $(CH_2)_3$
 N_H
 $(CH_2)_4$
 N_H
 N_H

RN 675606-40-3 HCAPLUS

CN Pentanamide, 2-(acetylamino)-N-[3-[(4-aminobutyl)amino]propyl]-5-[(aminoiminomethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_{2N}$$
 N_{H}
 $(CH_{2})_{3}$
 N_{H}
 $(CH_{2})_{4}$
 N_{H}
 $(CH_{2})_{4}$
 N_{H}

REFERENCE COUNT:

41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2003:4310 HCAPLUS

DOCUMENT NUMBER:

139:30604

TITLE:

L-Arginyl-3,4-spermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo

is chaemia without suppressing synaptic transmission

AUTHOR(S):

Morrison, Barclay, III; Pringle, Ashley K.; McManus, Terence; Ellard, John; Bradley, Mark; Signorelli, Francesco; Iannotti, Fausto;

Sundstrom, Lars E.

CORPORATE SOURCE:

Division of Clinical Neurosciences, School of Medicine, Bassett Crescent East, University of

Southampton, Southampton, SO16 7PX, UK

SOURCE:

British Journal of Pharmacology (2002), 137(8),

1255-1268

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER:

Nature Publishing Group

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB 1 Stroke is the third most common cause of death in the world, and there is a clear need to develop new therapeutics for the stroke victim. To address this need, we generated a combinatorial library of polyamine compds. based on sFTX-3.3 toxin from which L-Arginyl-3,4-spermidine (L-Arg-3,4) emerged as a lead neuroprotective compound. In the present study, we have extended earlier results to examine the compound's neuroprotective actions in greater detail. 2 In an in vitro ischemia model, L-Arg-3,4 significantly reduced CA1 cell death when administered prior to induction of 60 min of ischemia as well as when administered immediately after ischemia. Surprisingly, L-Arg-3,4 continued to prevent cell death significantly when administration was delayed for as long as 60

min after ischemia. 3 L-Arg-3,4 significantly reduced cell death in excitotoxicity models mediated by glutamate, NMDA, AMPA, or kainate. Unlike glutamate receptor antagonists, 300 μM L-Arg-3,4 did not suppress synaptic transmission as measured by evoked responses in acute hippocampal slices. 4 L-Arg-3,4 provided significant protection, in vitro, in a superoxide mediated injury model and prevented an increase of superoxide production after AMPA or NMDA stimulation. It also decreased nitric oxide production after in vitro ischemia and NMDA stimulation, but did so without inhibiting nitric oxide synthase directly. 5 Furthermore, L-Arg-3,4 was significantly neuroprotective in an in vivo model of global forebrain ischemia, without any apparent neurol. side-effects. 6 Taken together, these results demonstrate that L-Arg-3,4 is protective in several models of neurodegeneration and may have potential as a new therapeutic compound for the treatment of stroke, trauma, and other neurodegenerative diseases.

CC 1-11 (Pharmacology)

ST arginylspermidine neuroprotective forebrain ischemia stroke

IT Glutamate receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AMPA-binding; arginylspermidine is neuroprotective in several in vitro
models of neurodegeneration and in vivo ischemia without suppressing
synaptic transmission)

IT Brain, disease

(forebrain, ischemia; arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT Brain

(hippocampus, sector CA1, cell death inhibition; arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT Cytoprotective agents

(neuroprotective; arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT Toxicity

(neurotoxicity, excitotoxicity; arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT Brain, disease

(stroke; arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT Neurotransmission

(synaptic; arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT Nerve

(toxicity, excitotoxicity; arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT 56-86-0, L-Glutamic acid, biological studies 487-79-6, Kainic acid 6384-92-5 10102-43-9, Nitric oxide,

biological studies 11062-77-4, Superoxide

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT 191277-14-2

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

IT 56-86-0, L-Glutamic acid, biological studies 487-79-6,

Kainic acid 6384-92-5 10102-43-9, Nitric oxide,

biological studies 11062-77-4, Superoxide

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

RN 56-86-0 HCAPLUS

CN L-Glutamic acid (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 487-79-6 HCAPLUS

CN 3-Pyrrolidineacetic acid, 2-carboxy-4-(1-methylethenyl)-, (2S,3S,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

$$HO_2C$$
 S
 S
 S
 S
 S
 S
 S

RN 6384-92-5 HCAPLUS

CN D-Aspartic acid, N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 10102-43-9 HCAPLUS

CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N = 0

RN 11062-77-4 HCAPLUS

CN Superoxide (8CI, 9CI) (CA INDEX NAME)

0=0

IT 191277-14-2

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(arginylspermidine is neuroprotective in several in vitro models of neurodegeneration and in vivo ischemia without suppressing synaptic transmission)

RN 191277-14-2 HCAPLUS

CN Pentanamide, 2-amino-N-[3-[(4-aminobutyl)amino]propyl]-5-[(aminoiminomethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1999:404918 HCAPLUS

DOCUMENT NUMBER:

131:59135

TITLE:

Preparation of amino acid derivatives as

neuroprotective agents

INVENTOR(S):

Pringle, Ashley Ker; Bradley, Mark
; Sundstrom, Lars Eric; Iannotti,

Fausto

PATENT ASSIGNEE(S):

University of Southampton, UK

SOURCE:

PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT	NO.		KI	ND	DATE			A:	PPLI	CATIO	и ис	o.	DATE			
WO	WO 9931049			A1 19990624				WO 1998-GB3775 1998121									
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                                           PT 1998-960031
                       т
                            20030930
     PT 1040096
                                                             19981216
                                           ES 1998-960031
     ES 2201563
                       Т3
                            20040316
                                                             19981216
                                           CA 1999-2355880
                                                             19990616
     CA 2355880
                       AΑ
                            20000622
                                           WO 1999-GB1719
     WO 2000035941
                       Α2
                            20000622
                                                             19990616
                            20011004
     WO 2000035941
                       AЗ
         W: CA, US
                    CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
         RW: AT, BE,
             PT, SE
                                           EP 1999-936759
                            20011017
                                                             19990616
     EP 1144434
                       A2
                            20020529
     EP 1144434
                       AЗ
                     CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE
         R: AT, BE,
                            20000815
                                           NO 2000-3075
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     NO 2000003075
                       Α
                                           HK 2000-108125
                            20031003
                                                             20001215
     HK 1029331
                       Α1
                                        GB 1997-26569
                                                             19971216
PRIORITY APPLN. INFO.:
                                                          Α
                                        WO 1998-GB3775
                                                             19981216
                                                          W
                                        WO 1999-GB1719
                                                             19990616
                                                          W
                         MARPAT 131:59135
OTHER SOURCE(S):
    Amino acid derivs. Q-Ra-C*H(NR2R3)CO-Zn-NR1-Rb-NH-Rc-NH-W [Q = amidino,
AB
     cyano, or amino group; Ra, Rb, Rc = (un) substituted alkylene, alkenylene;
     R2, R3 = H, R, RCO, RO2C, RNHCO (R = (un) substituted alkyl or aryl); the
     chiral atom indicated by the asterisk is in the L configuration; Z is an
     amino acid residue; n = 0, 1; R1 = H, (un) substituted alkyl or aryl; W =
     H, alkyl, aryl] were prepared as neuroprotectants.
                                                         Thus,
     N1-L-arginylspermidine, prepared by coupling of resin-bound spermidine
     derivative with protected arginine, followed by deprotection/cleavage using
     TFA-phenol-water-triisopropylsilane-1,2-ethanedithiol, showed 99.4 %
     protection (relative to control hypoxia in CA1 pyramidal cell layer).
     ICM C07C237-10
TC
     ICS C07C257-14; A61K031-155; A61K031-16
CC
     34-2 (Amino Acids, Peptides, and Proteins)
     arginylspermidine prepn neuroprotectant; spermidine arginyl prepn
ST
     neuroprotectant
IT
     Structure-activity relationship
        (neuroprotectant; preparation of amino acid derivs. as neuroprotective
        agents)
     Cytoprotective agents
ΙT
        (neuroprotectants; preparation of amino acid derivs. as neuroprotective
        agents)
IT
     Ischemia
        (preparation of amino acid derivs. as neuroprotective agents)
IT
     Amino acids, preparation
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of amino acid derivs. as neuroprotective agents)
ΙT
     134951-15-8P 191277-14-2P 191277-15-3P
     227758-27-2P 227758-28-3P 227758-29-4P
     227758-31-8P 227758-32-9P 227758-33-0P
     227758-34-1P 227758-35-2P 227758-36-3P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of amino acid derivs. as neuroprotective agents)
TT
     227758-40-9 227758-41-0 227767-50-2
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of amino acid derivs. as neuroprotective agents)

IT 110-60-1, 1,4-Butanediamine 156-87-6

227758-37-4D, resin-bound

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of amino acid derivs. as neuroprotective agents)

IT 227758-39-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amino acid derivs. as neuroprotective agents)

IT 134951-15-8P 191277-14-2P 191277-15-3P

227758-27-2P 227758-28-3P 227758-29-4P

227758-31-8P 227758-32-9P 227758-33-0P

227758-34-1P 227758-35-2P 227758-36-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid derivs. as neuroprotective agents)

RN 134951-15-8 HCAPLUS

CN Hexanamide, 2,6-diamino-N-[3-[(4-aminobutyl)amino]propyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_4$
 N
 H
 $(CH_2)_3$
 N
 H
 $(CH_2)_4$
 NH_2

RN 191277-14-2 HCAPLUS

CN Pentanamide, 2-amino-N-[3-[(4-aminobutyl)amino]propyl]-5-[(aminoiminomethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)$$
 4 (CH_2) 3 (CH_2) 3 (CH_2) 3 (CH_2) 3 (CH_2) 3 (CH_2) 1 (CH_2) 1

RN 191277-15-3 HCAPLUS

CN Pentanamide, 2-amino-N-[3-[(4-aminobutyl)amino]propyl]-5-[(aminoiminomethyl)amino]-, (2R)- (9CI) (CA INDEX NAME)

$$H_2N$$
 $(CH_2)_4$
 N
 H
 $(CH_2)_3$
 N
 H
 NH_2

RN 227758-27-2 HCAPLUS

CN Hexanamide, 2,6-diamino-N-[3-[(4-aminobutyl)amino]propyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_4$
 R
 N
 H
 $(CH_2)_3$
 N
 H
 $(CH_2)_4$
 NH_2

RN 227758-28-3 HCAPLUS

CN Pentanamide, 2,5-diamino-N-[3-[(4-aminobutyl)amino]propyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_3$
 N
 H
 $(CH_2)_4$
 NH_2

RN 227758-29-4 HCAPLUS

CN Pentanamide, 2,5-diamino-N-[3-[(4-aminobutyl)amino]propyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_3$
 R
 $(CH_2)_3$
 N
 H
 $(CH_2)_4$
 NH_2

RN 227758-31-8 HCAPLUS

CN L-Phenylalaninamide, L-arginyl-N-[3-[(4-aminobutyl)amino]propyl]-, tetrakis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 227758-30-7

CMF C22 H40 N8 O2

Absolute stereochemistry.

$$H_2N$$
 NH
 $(CH_2)_3$
 S
 NH_2
 $(CH_2)_3$
 $(CH_2)_4$
 NH_2

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 227758-32-9 HCAPLUS

CN L-Phenylalaninamide, N6-(aminoiminomethyl)-L-lysyl-N-[3-[(4-aminobutyl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 NH
 $(CH_2)_4$
 S
 NH_2
 $(CH_2)_3$
 $(CH_2)_4$
 NH_2
 $(CH_2)_4$
 $(CH_2)_4$

RN 227758-33-0 HCAPLUS

CN L-Tyrosinamide, L-arginyl-N-[3-[(4-aminobutyl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 227758-34-1 HCAPLUS

L-Tryptophanamide, L-arginyl-N-[3-[(4-aminobutyl)amino]propyl]- (9CI) (CA CN INDEX NAME)

Absolute stereochemistry.

RN

227758-35-2 HCAPLUS Glycinamide, L-arginyl-N-[3-[(4-aminobutyl)amino]propyl]-2-phenyl- (9CI) CN (CA INDEX NAME)

Absolute stereochemistry.

227758-36-3 HCAPLUS RN

Pentanamide, 2-amino-N-[3-[(4-aminobutyl)amino]propyl]-5-CN [(aminocarbonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

227758-40-9 227758-41-0 227767-50-2 IT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of amino acid derivs. as neuroprotective agents)

227758-40-9 HCAPLUS RN

Pentanediamide, 2-amino-N1-[3-[(4-aminobutyl)amino]propyl]-, (2S)- (9CI) CN (CA INDEX NAME)

$$H_2N$$
 N
 H_2
 N
 H_2
 N
 H
 N
 H
 N
 H
 N
 H
 N
 H
 N
 H

RN 227758-41-0 HCAPLUS

CN Pentanamide, 2-amino-N-[4-[(4-aminobutyl)amino]butyl]-5-[(aminoiminomethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$H_2N$$
 $(CH_2)_4$
 N
 H
 $(CH_2)_4$
 N
 H
 $(CH_2)_4$
 N
 H
 NH_2

RN 227767-50-2 HCAPLUS

CN Pyridinepropanamide, α -amino-N-[3-[(4-aminobutyl)amino]propyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{O} & \text{NH}_2 \\ \parallel & \parallel & \parallel \\ \text{H}_2\text{N--} \text{(CH}_2)}_4 - \text{NH--} \text{(CH}_2)}_3 - \text{NH--} \text{C--} \text{CH--} \text{CH}_2 - \text{D1} \end{array}$$

IT 110-60-1, 1,4-Butanediamine 156-87-6

227758-37-4D, resin-bound

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of amino acid derivs. as neuroprotective agents)

RN 110-60-1 HCAPLUS

CN 1,4-Butanediamine (8CI, 9CI) (CA INDEX NAME)

 $H_2N - (CH_2)_4 - NH_2$

RN 156-87-6 HCAPLUS

CN 1-Propanol, 3-amino- (8CI, 9CI) (CA INDEX NAME)

H2N-CH2-CH2-CH2-OH

RN 227758-37-4 HCAPLUS

CN 13-0xa-2,6,11-triazapentadecanoic acid, 6-[2-amino-1-[4-[(benzoyloxy)carbonyl]phenoxy]-2-oxoethyl]-14,14-dimethyl-12-oxo-,

9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

IT 227758-39-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amino acid derivs. as neuroprotective agents)

RN 227758-39-6 HCAPLUS

CN 1,3-Cyclohexanedione, 2-[1-[(3-hydroxypropyl)amino]ethylidene]-5,5-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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